Cognition and symptoms

Introduction

Schizophrenia is characterised by positive, negative and disorganised symptoms. Positive symptoms are a well-documented feature of the disorder and arguably the are most recognisable symptoms. Positive symptoms refer to experiences additional to what would be considered normal experience, such as hallucinations and delusions. Hallucinations are sensory perceptions which may be auditory or visual; delusions are false beliefs. Negative symptoms refer to processes featuring an absence of normal function, and include blunted affect, impoverished thinking, alogia, asociality, avolition and anhedonia. Alogia is often manifested as poverty of speech, asociality involves reduced social interaction, avolition refers to poor hygiene and reduced motivation, while anhedonia is defined as an inability to experience pleasure. Symptoms of disorganisation involve bizarre behavior and disorganised thought and speech. Depressive symptoms are also common, with many individuals experiencing depression after the psychotic episode.

Cognitive deficits are also a core feature of schizophrenia. These deficits may be present in chronic patients, as well as prior to onset of the disorder and during its early and acute stages. Cognitive deficits may be associated with specific symptoms as well as functional impairment.

Method

We have included only systematic reviews with detailed literature search, methodology, and inclusion/exclusion criteria that were published in full text, in English, from the year 2000. Reviews were identified by searching the databases MEDLINE, EMBASE, and PsycINFO. Reviews with pooled data are prioritized for inclusion. Reviews reporting fewer than 50% of items on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA¹) checklist have been



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excluded from the library. The evidence was graded guided by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach². The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

Results

We found 29 systematic reviews that met our inclusion criteria³⁻³¹.

Overall symptoms

- Moderate to high quality evidence shows that more severe overall symptoms are associated with lower prospective memory performance.
- Moderate to high quality evidence suggests an association between overall symptom severity and lower levels of insight.
- Moderate quality evidence suggests an association with poor executive functioning, impaired facial emotion perception, social perception, Theory of Mind, facial recognition and emotion processing.

Positive symptoms

- Moderate to high quality evidence suggests an association between more severe positive symptoms and lower levels of insight, attention/vigilance, reasoning and problem solving.
- Moderate quality evidence suggests an association with lower non-emotional recognition, self-recognition, psychomotor speed, executive functioning, and Theory of Mind.
- Moderate quality evidence suggests increased semantic priming in patients with thought disorder compared with controls.
- Moderate to low quality evidence suggests more impaired performance on verbal fluency and naming tasks in patients with

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thought disorder compared with patients without thought disorder.

 Moderate to low quality evidence suggests an association between more severe positive symptoms and reduced verbal list learning, and digit span performance.

Negative symptoms

 Moderate to high quality evidence finds an association between more severe negative symptoms and poorer language fluency, IQ, attention, memory, learning, speed of processing, reasoning, executive functioning, insight, social cognition, and olfaction.

Disorganisation symptoms

- Moderate to high quality evidence suggests an association between more severe disorganised symptoms and lower IQ, attention, executive functioning, speed of processing, and memory (but not verbal working memory).
- Moderate to high quality evidence suggests an association with lower reasoning and problem-solving ability.

Other symptoms

- Moderate to high quality evidence suggests increased depression may be associated with increased levels of insight.
- Moderate to high quality evidence suggests a small, decreased risk of aggression with better cognitive functioning. This effect is apparent for global cognition and insight. There were no significant relationships with memory, attention, executive functioning, or visual-spatial reasoning.



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Bora E, Yucel M, Pantelis C

Cognitive functioning in schizophrenia, schizoaffective disorder and affective psychoses: meta-analytic study

The British Journal of Psychiatry 2009; 195: 475-482

View review abstract online

Comparison	Cognitive functioning in people with schizophrenia vs. people with affective psychosis or schizoaffective disorder. Note: the schizophrenia group had more males, with a younger mean age and with fewer years of education, which may account for any observed effects.
Summary of evidence	Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) suggests people with schizophrenia with high levels of negative symptoms may show the greatest impairments in memory and executive functioning compared with people with schizoaffective disorder/affective psychosis. Patients with high levels of either positive or negative symptoms may show the greatest impairments in psychomotor speed.

Memory

Meta-regression shows that people with schizophrenia who had highest levels of negative symptoms showed the greatest executive functioning impairments compared with people with schizoaffective / affective psychosis;

5 studies, $^{+}B = 0.23$, SE = 10, p = 0.02

Executive Functioning

Meta-regression shows that people with schizophrenia who had highest levels of negative symptoms showed the greatest executive functioning impairments compared with people with schizoaffective/affective psychosis;

6 studies, B = 0.41, SE = 0.09, *p* < 0.001

Psychomotor speed

Meta-regression shows that people with schizophrenia who had highest levels of positive or negative symptoms showed the greatest psychomotor impairments compared with people with

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schizoaffective/ affective psychosis;	
Positive symptoms: 20 studies, $B = 0.59$, $SE = 0.29$, $p = 0.04$	
Negative symptoms: 6 studies, $B = 0.39$, $SE = 0.09$, $p < 0.001$	
Consistency in results [‡]	Unable to assess; no measure of consistency is reported
Precision in results [§]	Unable to assess; no measure of precision is reported
Directness of results	Direct

Bora E, Binnur Akdede B, Alptekin K

Neurocognitive impairment in deficit and non-deficit schizophrenia: a meta-analysis

Psychological Medicine 2017; 47: 2401-13

View review abstract online

Comparison	Cognitive functioning in people with deficit schizophrenia vs. people with non-deficit schizophrenia. Both groups were also compared to controls.
Summary of evidence	Moderate to high quality evidence (large samples, mostly inconsistent, mostly precise, direct) suggests people with deficit schizophrenia are more impaired than people with non-deficit schizophrenia on measures of global cognition, memory, executive functioning, processing speed, attention, language, social cognition and olfaction.

Global cognition

Significant, medium-sized effect of poorer global cognition in people with deficit schizophrenia compared to people with non-deficit schizophrenia;

21 studies, N = 2,287, d = 0.47, 0.37 to 0.58, p < 0.001, $l^2 = 23\%$, p = 0.17

Significant, large effects of poorer global cognition in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;

Deficit: 12 studies, N = 1,210, d = 1.35, 95%Cl 1.14 to 1.56, p < 0.001, l² = 62%, p = 0.002

Non-deficit: 12 studies, N = 1,441, d = 0.91, 95%Cl 0.75 to 1.06, p < 0.001, $l^2 = 50\%$, p = 0.02

Memory

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Significant, small effects of poorer memory in people with deficit schizophrenia compared to people with non-deficit schizophrenia;
Verbal memory: 12 studies, N = 1,698, d = 0.34, 95%Cl 0.16 to 0.51, p < 0.001, l ² = 61%, p = 0.004
Visual memory: 10 studies, N = 789, d = 0.27, 95%Cl 0.13 to 0.42, p < 0.001, l ² = 0%, p = 0.90
Working memory: 9 studies, N = 1,428, $d = 0.24$, 95%Cl 0.11 to 0.37, $p < 0.001$, $l^2 = 14\%$, $p = 0.32$
Significant, large effects of poorer memory in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;
Verbal memory
Deficit: 8 studies, N = 962, $d = 1.43$, 95%Cl 1.23 to 1.63, $p < 0.001$, $l^2 = 39\%$, $p = 0.12$
Non-deficit: 8 studies, N = 1,116, $d = 1.19$, 95%Cl 1.03 to 1.35, $p < 0.001$, $l^2 = 38\%$, $p = 0.12$
Visual memory
Deficit: 8 studies, N = 962, $d = 1.17$, 95%Cl 0.87 to 1.47, $p < 0.001$, l ² = 72%, $p < 0.001$
Non-deficit: 8 studies, N = 1,116, $d = 0.78$, 95%Cl 0.66 to 0.91, $p < 0.001$, $l^2 = 0$ %, $p = 0.43$
Working memory
Deficit: 3 studies, N = 328, $d = 1.04$, 95%Cl 0.65 to 1.43, $p < 0.001$, $l^2 = 61$ %, $p = 0.07$
Non-deficit: 3 studies, N = 343, $d = 1.00$, 95%Cl 0.71 to 1.30, $p < 0.001$, $l^2 = 46\%$, $p = 0.16$
Executive Functioning
Executive Functioning Significant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia;
Executive Functioning Significant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia; Executive functioning: 16 studies, N = 1,928, d = 0.39, 95%CI 0.23 to 0.55, p < 0.001, l ² = 54%, p = 0.004
Executive Functioning Significant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia; Executive functioning: 16 studies, N = 1,928, d = 0.39, 95%Cl 0.23 to 0.55, p < 0.001, l ² = 54%, p = 0.004 TMT B: 9 studies, N = 832, d = 0.53, 95%Cl 0.29 to 0.76, p < 0.001, l ² = 58%, p = 0.01
Executive FunctioningSignificant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia;Executive functioning: 16 studies, N = 1,928, d = 0.39, 95%Cl 0.23 to 0.55, p < 0.001, l² = 54%, p = 0.004TMT B: 9 studies, N = 832, d = 0.53, 95%Cl 0.29 to 0.76, p < 0.001, l² = 58%, p = 0.01
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Executive Functioning Significant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia; Executive functioning: 16 studies, N = 1,928, $d = 0.39$, 95%CI 0.23 to 0.55, $p < 0.001$, $l^2 = 54\%$, $p = 0.004$ TMT B: 9 studies, N = 832, $d = 0.53$, 95%CI 0.29 to 0.76, $p < 0.001$, $l^2 = 58\%$, $p = 0.01$ Stroop interference: 5 studies, N = 447, $d = 0.49$, 95%CI 0.31 to 0.68, $p < 0.001$, $l^2 = 2\%$, $p = 0.40$ WCST categories: 8 studies, N = 1,433, $d = 0.44$, 95%CI 0.20 to 0.68, $p < 0.001$, $l^2 = 73\%$, $p < 0.001$ WCST preservative: 10 studies, N = 1,517, $d = 0.39$, 95%CI 0.21 to 0.57, $p < 0.001$, $l^2 = 54\%$, $p = 0.02$
Executive FunctioningSignificant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia;Executive functioning: 16 studies, N = 1,928, $d = 0.39$, 95%Cl 0.23 to 0.55, $p < 0.001$, $l^2 = 54\%$, $p = 0.004$ TMT B: 9 studies, N = 832, $d = 0.53$, 95%Cl 0.29 to 0.76, $p < 0.001$, $l^2 = 58\%$, $p = 0.01$ Stroop interference: 5 studies, N = 447, $d = 0.49$, 95%Cl 0.31 to 0.68, $p < 0.001$, $l^2 = 2\%$, $p = 0.40$ WCST categories: 8 studies, N = 1,433, $d = 0.44$, 95%Cl 0.20 to 0.68, $p < 0.001$, $l^2 = 73\%$, $p < 0.001$ WCST preservative: 10 studies, N = 1,517, $d = 0.39$, 95%Cl 0.21 to 0.57, $p < 0.001$, $l^2 = 54\%$, $p = 0.02$ Significant, large effects of poorer executive functioning in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;
Executive FunctioningSignificant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia;Executive functioning: 16 studies, N = 1,928, $d = 0.39$, 95%Cl 0.23 to 0.55, $p < 0.001$, $l^2 = 54\%$, $p = 0.004$ TMT B: 9 studies, N = 832, $d = 0.53$, 95%Cl 0.29 to 0.76, $p < 0.001$, $l^2 = 58\%$, $p = 0.01$ Stroop interference: 5 studies, N = 447, $d = 0.49$, 95%Cl 0.31 to 0.68, $p < 0.001$, $l^2 = 2\%$, $p = 0.40$ WCST categories: 8 studies, N = 1,433, $d = 0.44$, 95%Cl 0.20 to 0.68, $p < 0.001$, $l^2 = 73\%$, $p < 0.001$ WCST preservative: 10 studies, N = 1,517, $d = 0.39$, 95%Cl 0.21 to 0.57, $p < 0.001$, $l^2 = 54\%$, $p = 0.02$ Significant, large effects of poorer executive functioning in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls; Deficit: 10 studies, N = 1,030, $d = 1.23$, 95%Cl 1.02 to 1.44, $p < 0.001$, $l^2 = 52\%$, $p = 0.03$
Executive FunctioningSignificant, medium-sized effects of poorer executive functioning in people with deficit schizophrenia compared to people with non-deficit schizophrenia;Executive functioning: 16 studies, N = 1,928, $d = 0.39$, 95%CI 0.23 to 0.55, $p < 0.001$, $l^2 = 54\%$, $p = 0.004$ TMT B: 9 studies, N = 832, $d = 0.53$, 95%CI 0.29 to 0.76, $p < 0.001$, $l^2 = 58\%$, $p = 0.01$ Stroop interference: 5 studies, N = 447, $d = 0.49$, 95%CI 0.31 to 0.68, $p < 0.001$, $l^2 = 2\%$, $p = 0.40$ WCST categories: 8 studies, N = 1,433, $d = 0.44$, 95%CI 0.20 to 0.68, $p < 0.001$, $l^2 = 73\%$, $p < 0.001$ WCST preservative: 10 studies, N = 1,517, $d = 0.39$, 95%CI 0.21 to 0.57, $p < 0.001$, $l^2 = 54\%$, $p = 0.02$ Significant, large effects of poorer executive functioning in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls; Deficit: 10 studies, N = 1,030, $d = 1.23$, 95%CI 1.02 to 1.44, $p < 0.001$, $l^2 = 52\%$, $p = 0.03$ Non-deficit: 10 studies, N = 1,162, $d = 1.00$, 95%CI 0.85 to 1.14, $p < 0.001$, $l^2 = 25\%$, $p = 0.21$

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Significant, medium-sized effects of poorer processing speed in people with deficit schizophrenia compared to people with non-deficit schizophrenia;

Processing speed: 14 studies, N = 1,855, d = 0.43, 95%Cl 0.26 to 0.60, p < 0.001, l² = 59%, p = 0.003

TMT A: 8 studies, N = 793, d = 0.44, 95%Cl 0.15 to 0.74, p = 0.003, $l^2 = 71\%$, p < 0.001

Symbol coding: 5 studies, N = 1,171, d = 0.52, 95%Cl 0.33 to 0.71, p < 0.001, l² = 46%, p = 0.12

Significant, large effects of poorer processing speed in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;

Deficit: 6 studies, N = 822, d = 1.26, 95%CI 0.68 to 1.83, p < 0.001, I² = 92%, p < 0.001

Non-deficit: 6 studies, N = 907, d = 0.80, 95%Cl 0.44 to 1.16, p < 0.001, $l^2 = 83\%$, p < 0.001

Attention

Significant, medium-sized effect of poorer attention in people with deficit schizophrenia compared to people with non-deficit schizophrenia;

Attention: 9 studies, N = 1,271, d = 0.42, 95%CI 0.24 to 0.60, p < 0.001, I² = 45%, p = 0.07

Significant, large effect of poorer attention in people with deficit schizophrenia compared to controls and a medium-sized effect in people with non-deficit schizophrenia compared to controls;

Deficit: 7 studies, N = 869, d = 1.19, 95%Cl 0.80 to 1.58, p < 0.001, l² = 84%, p < 0.001

Non-deficit: 7 studies, N = 990, d = 0.68, 95%CI 0.50 to 0.87, p < 0.001, l² = 45%, p = 0.09

Language

Significant, medium-sized effects of poorer language fluency in people with deficit schizophrenia compared to people with non-deficit schizophrenia;

Overall fluency: 9 studies, N = 1,374, d = 0.60, 95%Cl 0.42 to 0.77, p < 0.001, l² = 47%, p = 0.06

Letter fluency: 9 studies, N = 1,374, d = 0.58, 95%Cl 0.40 to 0.77, p < 0.001, $l^2 = 51\%$, p = 0.04

Semantic fluency: 6 studies, N = 1,217, d = 0.54, 95%CI 0.36 to 0.72, p < 0.001, l² = 40%, p = 0.14

Significant, large effects of poorer language fluency in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;

Deficit: 6 studies, N = 636, d = 1.53, 95%Cl 1.34 to 1.71, p < 0.001, $l^2 = 0\%$, p = 0.69

Non-deficit: 6 studies, N = 738, d = 0.79, 95%Cl 0.64 to 0.94, p < 0.001, $l^2 = 0\%$, p = 0.55

Social cognition

Significant, medium-sized effects of poorer social cognition in people with deficit schizophrenia compared to people with non-deficit schizophrenia;

Social cognition: 9 studies, N = 1,215, *d* = 0.56, 95%CI 0.24 to 0.88, *p* < 0.001, I² = 81%, *p* < 0.001

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Label 3 studies, $N = 257$, $d = 0.93$,	, 95%Cl 0.54 to 1.31, <i>p</i> < 0.001, l ² = 55%, <i>p</i> = 0.11

Discrimination: 5 studies, N = 900, d = 0.36, 95%CI -0.02 to 0.73, I² = 75%, p = 0.003

Significant, large effects of poorer social cognition in people with deficit schizophrenia compared to controls and in people with non-deficit schizophrenia compared to controls;

Deficit: 6 studies, N = 426, d = 1.44, 95%Cl 0.64 to 2.24, p < 0.001, $l^2 = 95\%$, p < 0.001

Non-deficit: 6 studies, N = 485, d = 0.84, 95%Cl 0.59 to 1.09, p < 0.001, $l^2 = 57\%$, p = 0.06

Olfaction

Significant, large effect of poorer olfaction in people with deficit schizophrenia compared to people with non-deficit schizophrenia;

4 studies, N = 292, d = 0.84, 95%Cl 0.21 to 1.47, p = 0.009, l^2 = 83%, p < 0.001

Consistency in results	Mostly inconsistent
Precision in results	Mostly precise
Directness of results	Direct

Chan R, Li H, Cheung E, Gong QY Impaired facial emotion perception in schizophrenia: A meta-analysis	
Psychiatry Research 2010; 178: 381-390	
View review abstract online	
Comparison	Facial emotional perception and non-emotional facial or age recognition (control task) in people with schizophrenia vs. healthy controls.
Summary of evidence	Moderate quality evidence (unclear sample size, inconsistent, precise, direct) with a medium to large effect size, suggests that poorer performance on facial emotion perception may be associated with severity of negative symptoms and performance on non-emotional recognition tasks may be associated with severity of positive symptoms.
Facial emotional perception	
Greater negative symptom severity (measured by PANSS) was significantly associated with poorer	



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facial emotion perception, showing a large effect;	
Negative symptoms (PANSS): 7 studies, <i>d</i> = -1.11, 95%CI -1.63 to -0.60, <i>p</i> < 0.001, Q = 46.64	
No significant association was reported between facial emotion perception and negative symptoms (measured by SANS), and positive symptoms (measured by the PANSS or SAPS).	
Greater positive symptom severity (measured by PANSS) was significantly associated with poorer performance on facial recognition tasks, showing a medium to large effect;	
Positive symptoms (PANSS): 7 studies, <i>d</i> = -0.70, 95%CI -1.08 to -0.31, <i>p</i> < 0.001, Q = 24.98	
No association was reported with negative symptoms (measured by PANSS or SANS), or positive symptoms (measured by SAPS).	
Consistency	Inconsistent for group comparisons, unable to assess moderator analyses
Precision	Precise
Directness	Direct

Cohen A, Saperstein A, Gold J, Kirkpatrick B, Carpenter W, Buchanan R

Neuropsychology of the deficit syndrome: New data and meta-analysis of findings to date

Schizophrenia Bulletin 2007; 33(5): 1201-1212

View review abstract online

Comparison	Association between cognitive functioning and symptom dimensions in people with deficit schizophrenia (predominantly negative symptoms) vs. people with non-deficit schizophrenia.
Summary of evidence	Moderate to low quality evidence (unclear or large sample size, direct, unable to assess consistency or precision) suggests people with deficit schizophrenia may show greater neuropsychological impairment than people with non-deficit schizophrenia on; speeded and non-speeded tasks; tasks tapping language, global cognition, and social cognition.
	Overall neuropsychological processes
Authors state there was gr	eater neuropsychological impairment in people with deficit schizophrenia

compared with non-deficit schizophrenia;

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Sample sizes, Q and *p*-values are not reported

Language

Mean weighted ES (unspecified) = 0.51, 95%Cl -1.81 to 2.83

Global cognition

Mean weighted ES (unspecified) = 0.52, 95%CI 0.23 to 0.82

Social cognition

Mean weighted ES (unspecified) = 0.56, 95%CI -2.09 to 3.21

Olfactory discriminations

Mean weighted ES (unspecified) = 1.11, 95%CI not reported

Performance speed

The greater impairment in people with deficit schizophrenia compared with non-deficit schizophrenia was evident for both speeded and non-speeded tasks, with no significant differences in results across tasks;

 $Q_B = 0.17$, *p*-value reported as non-significant

Speeded tasks

8 studies, N = 467, 19 measures

Mean weighted ES (unspecified) = 0.46, 95%CI 0.26 to 0.67, Q_w = 4.95 *p*-value not reported

Non-speeded tasks

13 studies, N = 719, 90 measures

Mean weighted ES (unspecified) = 0.42, 95%CI 0.26 to 0.57, Q_w = 13.03 p-value not reported

Brain regions

The greater impairment in people with deficit schizophrenia compared with non-deficit schizophrenia was evident in tasks thought to tap frontal, parietal, temporal and other, non-specific brain regions, with no significant differences in results across regions;

 $Q_B = 8.89$, *p*-value not reported

Frontal lobe

9 studies, N = 533, 31 measures, *p*-values not reported

Mean weighted ES (unspecified) = 0.42, 95%CI 0.23 to 0.62, Q_w = 12.89

Parietal lobe

7 studies, N = 540, 16 measures *p*-values not reported

Mean weighted ES (unspecified) = 0.22, 95%CI 0.01 to 0.44, $Q_w = 1.30$

Temporal lobe

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9 studies, N = 533, 44 measures <i>p</i> -values not reported	
Mean weighted ES (unspecified) = 0.40, 95%CI 0.19 to 0.60, $Q_w = 4.81$	
Nonspecific brain regions	
7 studies, N = 463, 15 measures p -values not reported	
Mean weighted ES (unspecified) = 0.42, 95%CI 0.21 to 0.64, $Q_w = 5.53$	
Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Daban C, Martinez-Aran A, Torrent C, Tabarés-Seisdedos R, Balanzá-Martínez V, Salazar-Fraile J, Selva-Vera G, Vieta E

Specificity of cognitive deficits in bipolar disorder versus schizophrenia: A systematic review

Psychotherapy and Psychosomatics 2006; 75: 72-84

View review abstract online

Comparison	Association between symptoms and cognitive performance in people with schizophrenia vs. bipolar disorder.
Summary of evidence	Moderate to low quality evidence (small to medium-sized samples, unable to assess consistency or precision, direct) suggests increased positive or negative symptoms may be associated with decreased executive functioning. Increased negative symptoms may be associated with decreased verbal fluency.
Attention	
2 studies (N = 279) reported no difference between people with schizophrenia or bipolar disorder without psychotic symptoms.	

Executive functioning

1 study (N = 107) reported an association between increased negative symptoms and poorer executive functioning.

1 study (N = 108) reported that people with psychotic symptoms performed more poorly than those

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without psychotic symptoms.	
Language	
1 study (N = 94) reported an association between increased negative symptoms and worse verbal fluency.	
Consistency	Unable to assess; no measure of consistency is reported.
Precision	Unable to assess; no measure of precision is reported.
Directness	Direct

de Gracia Domingues M, Viechtbauer W, Simons C, van Os J

Are psychotic psychopathology and neurocognition orthogonal? A systematic review of their associations

Psychological Bulletin 2009; 135(1): 157-171

View review abstract online

Comparison	Association between cognitive functioning and symptom dimensions in people with non-affective psychosis.
Summary of evidence	Moderate to high quality evidence (unclear sample size, direct, consistent, precise) shows small to medium-sized associations between more severe negative symptoms and lower verbal fluency, IQ, attention, memory (but not verbal working memory), speed of processing and reasoning ability. There were small to medium size associations between more severe disorganised symptoms and lower IQ, attention, memory (but not verbal working memory), and speed of processing. Moderate quality evidence (inconsistent) also suggests an association with lower reasoning ability. Moderate quality evidence suggests a very weak association between more severe positive symptoms and lower speed of processing
	Executive functioning and verbal fluency
A significant medium assoc	siation between increased negative symptoms and lower verbal fluency;

23 studies, μ_p = -0.291, 95%CI -0.356 to -0.224, p = 0.00, I² = 42%

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No association between negative symptoms and executive control
10 studies, μ_p = -0.131, 95%Cl -0.265 to 0.008, p = 0.063, l ² = 56%
No association with positive or disorganised symptoms;
Positive symptoms and executive control: 9 studies, $\mu_p = 0.082$, 95%CI -0.017 to 0.179, $p = 0.10$
$l^2 = 7\%$
Positive symptoms and verbal fluency: 20 studies, μ_p = -0.035, 95%CI -0.101 to 0.031, p = 0.29
l ² = 17%
Disorganised symptoms and executive control: 7 studies, $\mu_p = -0.089$, 95%CI -0.202 to -0.026, $p = 0.13$, $l^2 = 20\%$
Disorganised symptoms and verbal fluency: 13 studies, μ_p = -0.092, 95%Cl -0.208 to 0.027, p = 0.13, l^2 = 61%
IQ
A significant medium association between increased negative symptoms and lower IQ;
13 studies, μ_p = -0.244, 95%Cl -0.333 to -0.151, p = 0.00, l ² = 52%
A significant medium association between increased disorganised symptoms and lower IQ;
6 studies, μ_p = -0.205, 95%Cl -0.327 to -0.076, p = 0.002, l ² = 45%
No association with positive symptoms;
10 studies, $\mu_p = 0.024$, 95%Cl -0.063 to 0.111, $p = 0.591$, $l^2 = 26\%$
Attention / vigilance
A significant weak association between increased negative symptoms and worse attention;
15 studies, μ_p = -0.134, 95%Cl -0.191 to -0.076, p = 0.00, l ² = 26%
A significant medium association between increased disorganised symptoms and worse attention;
6 studies, μ_p = -0.277, 95%Cl -0.392 to -0.154, p = 0.00, l ² = 34%
No association with positive symptoms;
11 studies, μ_p = -0.012, 95%Cl -0.054 to 0.003, p = 0.969, l ² = 0%
Memory
A significant small to medium association between increased negative symptoms and lower:
Verbal learning and memory;
20 studies, μ_p = -0.214, 95%Cl -0.279 to -0.146, p = 0.00, l ² = 54%
Visual learning and memory;

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 13 studies, μ_p = -0.126, 95%Cl -0.202 to -0.047, p = 0.001, l ² = 29%
No association with verbal working memory;
10 studies, μ_p = -0.07, 95%Cl -0.174 to 0.036, p = 0.194, l ² = 19%
A significant small to medium association between increased disorganised symptoms and lower:
Visual learning and memory;
6 studies, μ_p = -0.206, 95%CI -0.331 to -0.074, p = 0.002, I ² = 42%
Verbal learning and memory;
13 studies, μ_p = -0.169, 95%Cl -0.27 to -0.064, p = 0.001, l ² = 59%
No association between with verbal working memory;
5 studies, μ_p = -0.177, 95%CI -0.247 to 0.018, p = 0.09, I ² = 0%
No association with positive symptoms;
Verbal working memory: 9 studies, μ_p = -0.013, 95%CI -0.144 to 0.118, p = 0.843, I ² = 37%
Verbal learning and memory: 17 studies, μ_p = -0.021, 95%Cl -0.096 to 0.054, p = 0.578, l ² = 47%
Visual learning and memory: 9 studies, μ_p = -0.005, 95%CI -0.089 to 0.079, p = 0.91, I ² = 0%
Information processing
A significant weak association between increased negative symptoms and lower speed of processing;
23 studies, μ_p = -0.167, 95%CI -0.241 to -0.09, p = 0.00, I ² = 53%
A significant weak association between increased disorganised symptoms and lower speed of processing;
13 studies, μ_p = -0.171, 95%CI -0.275 to -0.062, p = 0.002, I ² = 56%
A significant very weak association between increased positive symptoms and lower speed of processing;
20 studies, μ_p = -0.089, 95%Cl -0.164 to -0.012, p = 0.023, l ² = 46%
Reasoning ability
A significant weak association between increased negative symptoms and lower reasoning and problem solving;
33 studies, μ_p = -0.140, 95%Cl -0.197 to -0.081, p = 0.00, l ² = 58%
A significant small to medium association between increased disorganised symptoms and lower reasoning and problem solving;
15 studies, μ_p = -0.197, 95%Cl -0.336 to -0.048, $p < p$ = 0.009, l ² = 81%

No association with positive symptoms;

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27 studies, μ_p = -0.013, 95%Cl -0.066 to 0.041, p = 0.639, l ² = 37%	
Consistency	Consistent apart from reasoning and problem solving with disorganised symptoms
Precision	Precise
Directness	Direct

Dibben CR, Rice C, Laws K, McKenna PJ

Is executive impairment associated with schizophrenic syndromes? A meta-analysis

Psychological Medicine 2009; 39(3): 381-392

View review abstract online

Comparison	Association between executive impairment and negative symptoms in people with schizophrenia.
Summary of evidence	Moderate to high quality evidence (unclear sample size, consistent in overall analysis, precise, direct) shows a weak association between more impaired executive function and increased negative symptoms. This association was increased in patients who were untreated or who were chronically hospitalised. Verbal fluency tasks report the strongest association.
	Moderate quality evidence (unable to assess consistency) shows a weak association between lower IQ and increased negative symptoms.
Executive impairment and negative symptoms	
Overall executive impairment	
• · · · ·	

Small effect size suggests an association of reduced executive function with negative symptoms in people with schizophrenia;

83 studies, N not reported, r = -0.21, 95%CI -0.24 to -0.18, p-value not reported, $Q_w = 321.84$, p < 0.0001

Excluding 21 outliers gave a similar effect, with homogenous results:

r = -0.20, 95%Cl -0.23 to -0.17, Q_w = NS

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Subgroup analyses Greater association of executive dysfunction and negative symptoms were reported for antipsychotic treated patients vs. patients who were not receiving treatment; Treated: 58 studies, r = -0.19, Untreated: 7 studies, r = -0.29 $Q_B = 6.28, p = 0.01$ Greater association of executive dysfunction and negative symptoms were reported for chronically hospitalized (persistent) patients vs. acutely ill patients; Acutely ill: 19 studies, r = -0.13, Chronically ill: 35 studies, r = -0.24 $Q_{\rm B} = 20.93, p = 0.0001$ No moderating effect of age: 80 studies, N not reported, p = 0.71No moderating effect of duration of illness: 72 studies, N not reported, p = 0.28Task specific executive impairment All tasks showed a small to medium size association with negative symptoms; Verbal fluency: 40 studies, r = -0.27 95%CI -0.31 to -0.23 Trail-making tasks B: 24 studies, r = -0.24, 95%CI -0.29 to -0.18 WCST, set-shifting: 43 studies, r = -0.16, 95%CI -0.20 to -0.13 Executive working memory: 13 studies, r = -0.14, 95%CI -0.22 to -0.07 Stroop/Hayling: 16 studies, r = -0.13, 95%CI -0.21 to -0.05 Significant between-group differences in effect sizes were reported between the cognitive tasks, with the association between negative symptoms and verbal fluency being the strongest and between negative symptoms and STROOP being the weakest. $Q_B = 42.27, p < 0.001$ General intellectual impairment: IQ Small effect size suggests an association of reduced intellectual function with negative symptoms; 30 studies, N not reported, r = -0.21, 95%Cl -0.26 to -0.17, $Q_w =$ not reported Excluding 6 outliers did not change results: r = -0.23, 95%CI -0.28 to -0.17, $Q_w =$ not reported Consistency Inconsistent where reported, apart from reduced overall analysis Precision Precise **Directness** Direct **Comparison 2** Association between executive impairment and disorganised symptoms in people with schizophrenia. Moderate to high guality evidence (unclear sample size, Summary of evidence consistent in overall analysis, precise, direct) shows a medium

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	association of more impaired executive function in people with schizophrenia with increased disorganised symptoms. This association was increased in patients who were older, who had a longer duration of illness, who were untreated or who were chronically hospitalized. TMT-B task reports the strongest association.
	Moderate quality evidence (unable to assess consistency) shows a weak association of lower IQ in people with schizophrenia with increased disorganised symptoms.
Execu	ative impairment and disorganised symptoms
	Overall executive impairment
Small effect size suggests an association of reduced executive function with disorganised symptoms in people with schizophrenia;	
40 studies, N not reported,	<i>r</i> = -0.17, 95%Cl -0.21 to -0.13, p-value not reported, Q _w = 148.14, <i>p</i> < 0.0001
Excluding 8 out	liers resulted in a medium effect with homogenous results:
<i>r</i> = -0.28, 95%Cl -0.33 to -0.23, Q _w = NS	
Subgroup analyses	
Greater association of executive impairment with disorganised symptoms in older people with schizophrenia;	
40 studies, N not reported, $p = 0.05$	
Greater association of executive impairment with disorganised symptoms in people with schizophrenia with a longer duration of illness;	
36 studies, N not reported, $p = 0.0006$	
Greater association of executive dysfunction and disorganised symptoms were reported for neuroleptic treated patients;	
Treated: 27 studies, $r = -0.22$, Untreated: 5 studies, $r = -0.14$	
$Q_B = 4.09, \rho = 0.04$	
Greater association of executive dysfunction and disorganised symptoms were reported for chronically hospitalized (persistent) patients;	
Acutely ill: 11 studies, $r = -0.12$, Chronically ill: 16 studies, $r = -0.28$	
	$Q_B = 18.46, p = 0.0001$
	Task specific executive impairment
All tasks showed a	small to medium size association with disorganised symptoms;
Trail-maki	ng task B: 10 studies, <i>r</i> = -0.31, 95%CI -0.40 to -0.22

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Executiv	ve working memory: 6 studies, r = -0.12, 95%CI -0.23 to -0.00
Verbal	fluency: 18 studies, r = -0.11 95%CI -0.17 to -0.05
Significant between-group with the association betwe between disor	differences in effect sizes were reported between the cognitive tasks, en disorganised symptoms and trail-making B being the strongest and ganised symptoms and verbal fluency being the weakest.
	Q _B = 33.71, <i>p</i> < 0.001
	General intellectual impairment: IQ
Small effect size sugge	sts an association of reduced intellectual function with disorganised symptoms;
N not repor	rted, <i>r</i> = -0.21, 95%CI -0.28 to -0.14, Q _w = not reported
Excluding 2 o	putliers, $r = -0.28$, 95%CI -0.35 to -0.19, $Q_w = not$ reported
Consistency	Consistent
Precision	Precise
Directness	Direct
Comparison 3	Association between executive impairment and positive symptoms in people with schizophrenia.
Summary of evidence	Moderate quality evidence (unclear sample size, inconsistent, precise, direct) suggests no association between executive functioning and positive symptoms.
Ex	ecutive impairment and positive symptoms
	Overall executive impairment
No association of reduced executive function with positive symptoms in people with schizophrenia,	
34 studies, N not reported, <i>r</i> = -0.01, 95%CI -0.04 to 0.05, p-value not reported, Q _w = 321.84, <i>p</i> < 0.0001	
	Excluding 4 outliers did not change results
r =	-0.02, 95%CI -0.03 to 0.07, Q _w = not reported
Consistency	Inconsistent
Precision	Precise
Directness	Direct

Stroop/Hayling: 10 studies, *r* = -0.29, 95%CI -0.38 to -0.21 WCST, set-shifting: 19 studies, *r* = -0.19, 95%CI -0.24 to -0.14

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Doughty OJ, Done DJ

Is semantic memory impaired in schizophrenia? A systematic review and meta-analysis of 91 studies

Cognitive Neuropsychiatry 2009; 14(6): 473-509

View review abstract online

Comparison	Semantic memory and symptom dimensions in people with schizophrenia.
Summary of evidence	Moderate to low quality evidence (unclear sample size, direct, imprecise, unable to assess consistency) suggests more impaired performance in people with schizophrenia with formal thought disorder compared with people with schizophrenia without thought disorder on verbal fluency and naming tasks, with no consistent differences for semantic associations, categorisation or priming tasks.
	The evidence also suggests more impaired performance in verbal fluency in people with schizophrenia with negative symptoms compared with people with schizophrenia without negative symptoms.
Semantic memory tasks	

More impairment in people with thought disorder compared with people without thought disorder for; Verbal fluency: 3 studies reported a difference, d = -1.12, 95%Cl -1.72 to -0.72, p not reported Naming tests: 4 studies reported a difference, d = -1.195 vs. -0.73 (Cls not reported), p = 0.046Inconsistent findings for;

Semantic association: 1 study reported a difference, 1 study reported no difference (no statistics) Categorisation: 1 study reported a difference, 1 study reported no difference (no statistics)

No difference for;

Semantic priming: 1 study reported no difference: d = 0.126 vs. d = 0.202, p = 0.12

More impairment in people with negative symptoms compared with people without negative symptoms in:

Verbal fluency: 2 studies, d = -1.006, 95%CI -1.43 to -0.58, p not reported







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Consistency	Unable to assess; no measure of consistency is reported
Precision	Imprecise
Directness	Direct

Forbes NF, Carrick LA, McIntosh AM, Lawrie SM Working memory in schizophrenia: a meta-analysis	
Psychological Medicine 2009; 39: 889-905 View review abstract online	
Comparison	Association between working memory and symptom dimensions in people with schizophrenia vs. controls.
Summary of evidence	Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) suggests that increased positive and negative symptoms may be associated with poorer performance on verbal list learning and digit span forwards and backwards tasks.
Association between memory and symptoms	
Meta-regression suggests lower verbal list learning (list 1) was associated with increased positive ($b = 0.09$, $p = 0.035$) and negative symptoms ($b = 0.13$, $p = 0.019$). Digit span forwards and backwards combined was also associated with both increased positive ($b = 0.154$, $p < 0.001$) and negative symptoms ($b = 0.139$, $Z = 3.75$, $p < 0.001$). Number of studies and number of participants not reported.	
Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Henry JD, Crawford JR

A meta-analytic review of verbal fluency deficits in schizophrenia relative

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to other neurocognitive deficits		
Cognitive Neuropsychiatry	² 2005; 10(1): 1-33	
View review abstract online		
Comparison	Association between phonemic and semantic fluency and symptom dimensions in people with schizophrenia.	
Summary of evidence	Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) suggests people with schizophrenia may show an association between greater phonemic fluency and reduced negative symptoms. No association was reported between symptoms and semantic fluency.	
Phonemic fluency		
A significant association is reported between better phonemic fluency and reduced overall symptoms (BPRS, 18 studies, $r = 0.57$, $p = 0.013$) and negative symptoms (SANS, 12 studies, $r = 0.70$, $p = 0.011$) but not positive symptoms (SAPS, 11 studies, $r = 0.17$, $p = 0.626$).		
Semantic fluency		
No association was reported between semantic fluency and overall symptoms on BPRS (10 studies, $r = 0.23$, $p = 0.531$) or negative symptoms on SANS (5 studies, $r = 0.54$, $p = 0.347$).		
Consistency	Unable to assess; no measure of consistency is reported	
Precision	Unable to assess; no measure of precision is reported	
Directness	Direct	

Irani F, Kalkstein S, Moberg E, Moberg P

Neuropsychological performance in older patients with schizophrenia: A meta-analysis of cross-sectional and longitudinal studies

Schizophrenia Bulletin 2010; 37(6): 1318-1326

View review abstract online

Comparison

Association between cognitive functioning and symptom





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	dimensions in older people with schizophrenia (mean age 64 years).
Summary of evidence	Moderate quality evidence (unclear sample size, unable to assess consistency or precision, direct) suggests that older people with schizophrenia may show an association between poorer global cognition and increased positive and negative symptoms.
Global cognition	
Greater global cognitive impairment was significantly associated with both increased severity of positive and negative symptoms (measured by PANSS) in older people with schizophrenia;	
Positive symptoms: 7 studies, $p < 0.01$	
Negative symptoms: 7 studies, $p < 0.01$	
Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Johnson-Selfridge M, Zalewski C

Moderator variables of executive functioning in schizophrenia: metaanalytic findings

Schizophrenia Bulletin 2001; 27(2): 305-316

View review abstract online

Comparison	Association between executive functioning and symptom severity in people with schizophrenia vs. controls.
Summary of evidence	Moderate to low quality evidence (unclear sample size, direct, unable to assess consistency or precision) suggests that poorer executive functioning may be associated with greater symptom severity.
Executive functioning	



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Meta-regression reports a significant, medium size effect of increased symptom severity on increased effect sizes between schizophrenia and controls;

Higher negative and positive symptom ratings on the SANS (10 studies, r = -0.69) and SAPS (9 studies, r = -0.67) was associated with greater impairment in people with schizophrenia compared with controls; p < 0.05. No significant association was reported between effect sizes and BPRS scores (15 studies, r = -0.11).

Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Kohler C, Walker J, Martin E, Healey K, Moberg P

Face emotion perception in schizophrenia: A meta-analytic review

Schizophrenia Bulletin 2010; 36(5): 1009-1019

View review abstract online

Comparison	Association between facial emotion perception and symptom severity in people with schizophrenia vs. controls.
Summary of evidence	Moderate to high quality evidence (large sample, direct, precise, inconsistent) suggests impaired facial emotion perception in people with schizophrenia. The results also suggest that impairment in facial emotion perception may be associated with greater symptom severity (but not PANSS).

Facial emotion processing

A large effect size suggests overall impaired facial emotion identification and differentiation in people with schizophrenia compared with controls;

Number of studies is unclear, N = 3,822, d = -0.91, 95%CI -0.97 to -0.84, Q_B = 275.7, p < 0.001

A significant association was reported between impaired facial emotion perception and greater overall symptom severity (BPRS), negative symptoms (SANS) and positive symptoms (SAPS);

SANS: 20 studies, Z = -4.13, *p* < 0.001

SAPS: 18 studies, Z = -4.48, *p* < 0.001

BPRS: 6 studies, Z = -3.08, p = 0.002





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No association was found for PANSS positive, negative, or total symptom scores.	
Consistency	Inconsistent for overall comparison, unable to assess subgroups
Precision	Precise
Directness	Direct

Lincoln TM, Lüllmann E, Rief W

Correlates and long-term consequences of poor insight in patients with schizophrenia. A systematic review

Schizophrenia Bulletin 2007; 33 (6): 1324-1342

View review abstract online

Comparison	Association between insight and symptoms in people with schizophrenia.
Summary of evidence	Moderate to low quality evidence (mixed sample sizes, direct, unable to assess consistency or precision) suggests people with schizophrenia may show an association between increased insight and reduced symptom severity, but worse depressive symptoms.
Insight, symptoms and hospitalisation	
8 studies (N = 1,157) reported a significant association between poorer insight and increased symptom severity (general psychopathology, BPRS scores, positive, negative, and depressive symptoms and anxiety).	
1 study (N = 74) reported an association between poorer insight regarding treatment and increased rehospitalisation, but no association between insight regarding mental health status and rehospitalisation.	
3 studies (N = 175) reported no association between insight, symptoms, and rehospitalisation.	
Insight and depression	

4 studies (N = 512) reported an association between increased insight and increased depressive symptoms, lower self-esteem (2 studies, N = 362) and positive and negative symptoms (1 study, N = 100).

1 study (N = 101 first-episode schizophrenia/ schizoaffective) reported an association between

Cognition and symptoms



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greater insight and increased depression and suicide at follow-up when using the Birchwood Scale, but no association using the PANSS.

1 study (N = 980) reported an association between increased insight and increased suicide events, but no association with depression. Increased insight as a function of treatment was associated with decreased risk of suicide.

1 study (N = 33) reported an association between lower insight/awareness of symptoms and increased depression (r = -0.46 - 0.58).

1 study (N = 74) reported no association between insight and suicidal tendency during a 1-year follow-up.

Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Mintz A, Dobson K, Romney D Insight in schizophrenia: a meta-analysis

Schizophrenia Research 2003; 61: 75-88

View review abstract online

Comparison	Association between insight (patient's awareness of the disorder) and symptom dimensions in people with schizophrenia.
Summary of evidence	Moderate to high quality evidence (medium to large samples, some inconsistency, some imprecision, direct) suggests increased global, positive and negative symptoms may be related to lower levels of insight of the disorder and its consequences. Conversely, increased depression is related to increased levels of insight.
	Global symptoms
A medium negative ass schizoj	ociation suggests that as global symptoms increase in patients with ohrenia, they may demonstrate less overall insight;
19 studies, N = 1,361: <i>r</i> =	= -0.27, $p < 0.001$, 95%CI -0.41 to -0.13, Q_w = not reported, $p > 0.05$
A	nd less insight for the following components;

Cognition and symptoms



 $\begin{aligned} & 31.24, \, p < 0.001 \\ \text{Awareness of social consequences: 2 studies, N = 251, } r = -0.27, \, p < 0.001, \, 95\%\text{CI} - 0.27 \text{ to} -0.27, \\ & Q_{w} = \text{non-significant} \\ \text{Awareness of need for treatment: 4 studies, N = 323, } r = -0.25, \, p < 0.001, \, 95\%\text{CI} - 0.25 \text{ to} -0.25, \, Q_{w} \\ & = \text{non-significant} \\ \text{Awareness of symptoms: 2 studies, N = 108, } r = -0.41, \, p < 0.001, \, 95\%\text{CI} - 0.61 \text{ to} -0.22, \, Q_{w} = \text{non-significant} \\ \end{aligned}$

Awareness of mental disorder: 8 studies, N = 742, r = -0.20, p < 0.001, 95%Cl -0.54 to 0.13, Q_w =

Attribution of symptoms: 2 studies, N = 108, r = -0.21, p < 0.05, 95%CI -0.43 to 0.01, Q_w = non-significant

Composite of awareness of mental disorder, awareness of social consequences of disorder and awareness of need for treatment: 14 studies, N = 926, r = -0.24, p < 0.001, 95%Cl -0.54 to 0.06, Q_w = 38.01, p < 0.001

Positive symptoms

A medium negative association suggests that as positive symptoms increase in patients with schizophrenia, they may demonstrate less overall insight;
22 studies, N = 1,616, r = -0.25, p < 0.001, 95%CI -0.64 to 0.13, Q _w = 92.32, p < 0.001
Note: Subgroup analysis suggests that this relationship was strongest in samples that were comprised of a large percentage of acutely psychotic patients.
And less insight for the following components;
Awareness of mental disorder: 9 studies, N = 686, r = -0.32, p < 0.001, 95%Cl -0.68 to 0.04, Q _w = 37.59, p < 0.001
Awareness of social consequences: 3 studies, N = 191, r = -0.33, p < 0.001, 95%CI -0.33 to -0.33, Q_w = non-significant
Awareness of the need for treatment: 2 studies, N =136, r = -0.31, p < 0.001, 95%CI -0.31 to -0.31, Q_w = non-significant
Awareness of symptoms: 3 studies, N = 100, r = -0.23, p < 0.01, 95%CI -0.23 to -0.23, Q _w = non-significant
Attribution of symptoms to disorder: 3 studies, N = 146, r = -0.16, p < 0.05, 95%CI -0.72 to 0.39, Q _w = 15.28, p < 0.001
Composite of awareness of mental disorder, awareness of social consequences of disorder and awareness of need for treatment: 9 studies, N = 807, r = -0.18, p < 0.001, 95%CI -0.35 to 0.00, Q _w = 16.02, p < 0.05
Negative symptoms

Cognition and symptoms



A medium negative association suggests that as negative symptoms increase in patients with schizophrenia, they may demonstrate less overall insight;
20 studies, N = 1487, r = -0.23, p < 0.001, 95%CI -0.48 to 0.02, Q _w = 47.69, p < 0.001
Note: Subgroup analysis suggests that this relationship was strongest in patients with an older age of onset of the disorder.
And less insight for the following components;
Awareness of mental disorder: 8 studies, N = 619, r = -0.20, p < 0.001, 95%Cl -0.45 to 0.04, Q _w = 18.63, p < 0.01
Awareness of social consequences: 2 studies, N = 125, r = -0.40, p < 0.001, 95%CI -0.40 to -0.40, Q_w = non-significant
Awareness of need for treatment: 2 studies, N = 136, r = -0.40, p < 0.001, 95%CI -0.40 to -0.40, Q _w = non-significant
Attribution of symptoms: 3 studies, N = 146, r = -0.33, p < 0.001, 95%CI -0.33 to -0.33, Q _w = non-significant
No significant association was reported between awareness of symptoms and negative symptoms;
2 studies, N = 71, r = -0.16, p > 0.05, 95%CI -0.16 to -0.16, Q _w = non-significant
Composite of awareness of mental disorder, awareness of social consequences of disorder and awareness of need for treatment: 11 studies, N = 800, r = -0.29, p < 0.001, 95%CI -0.63 to 0.04, Q _w =
38.68, <i>p</i> < 0.001
38.68, <i>p</i> < 0.001 Depressive symptoms
38.68, <i>p</i> < 0.001 Depressive symptoms A weak positive association suggests that as depressive symptoms increase in patients with schizophrenia, they may demonstrate more overall insight;
38.68, <i>p</i> < 0.001 Depressive symptoms <i>A weak positive association suggests that as depressive symptoms increase in patients with schizophrenia, they may demonstrate more overall insight;</i> 15 studies, N = 1,218, <i>r</i> = 0.18, <i>p</i> < 0.001, 95%CI -0.14 to 0.49, Q _w = 48.63, <i>p</i> < 0.001
38.68, <i>p</i> < 0.001 Depressive symptoms <i>A weak positive association suggests that as depressive symptoms increase in patients with schizophrenia, they may demonstrate more overall insight;</i> 15 studies, N = 1,218, <i>r</i> = 0.18, <i>p</i> < 0.001, 95%CI -0.14 to 0.49, Q _w = 48.63, <i>p</i> < 0.001 <i>And less insight for the following components;</i>
38.68, <i>p</i> < 0.001 Depressive symptoms <i>A weak positive association suggests that as depressive symptoms increase in patients with schizophrenia, they may demonstrate more overall insight;</i> 15 studies, N = 1,218, <i>r</i> = 0.18, <i>p</i> < 0.001, 95%Cl -0.14 to 0.49, Q _w = 48.63, <i>p</i> < 0.001 <i>And less insight for the following components;</i> Awareness of mental disorder: 7 studies, N = 579, <i>r</i> = 0.11, <i>p</i> < 0.01, 95%Cl -0.24 to 0.46, Q _w = 26.14, <i>p</i> < 0.001
$\begin{array}{l} \hline & \textbf{38.68, $p < 0.001} \\ \hline & \textbf{Depressive symptoms} \\ \hline & \textbf{A weak positive association suggests that as depressive symptoms increase in patients with schizophrenia, they may demonstrate more overall insight; \\ \hline & \textbf{15 studies, N = 1,218, $r = 0.18, $p < 0.001, $95\%Cl -0.14 to 0.49, $Q_w = 48.63, $p < 0.001$ \\ \hline & \textbf{And less insight for the following components;} \\ \hline & \textbf{Awareness of mental disorder: 7 studies, $N = 579, $r = 0.11, $p < 0.01, $95\%Cl -0.24 to 0.46, $Q_w = 26.14, $p < 0.001$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05$ \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05} \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05} \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05} \\ \hline & \textbf{Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to 0.52, $Q_w = 5.14, $p < 0.05} \\ \hline & Awareness of social consequences: 2 studies, $N = 121, $r = 0.21, $p < 0.01, $95\%Cl -0.09 to$
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$\begin{array}{c} 38.68, \ p < 0.001 \\ \hline \\ $
$\begin{array}{c} 38.68, \ p < 0.001 \\ \hline \textbf{Depressive symptoms} \\ \hline A \ weak \ positive \ association \ suggests \ that \ as \ depressive \ symptoms \ increase \ in \ patients \ with \ schizophrenia, \ they \ may \ demonstrate \ more \ overall \ insight; \\ 15 \ studies, \ N = 1,218, \ r = 0.18, \ p < 0.001, \ 95\% Cl \ -0.14 \ to \ 0.49, \ Q_w = 48.63, \ p < 0.001 \\ \ And \ less \ insight \ for \ the \ following \ components; \\ Awareness \ of \ mental \ disorder: \ 7 \ studies, \ N = 579, \ r = 0.11, \ p < 0.01, \ 95\% Cl \ -0.24 \ to \ 0.46, \ Q_w = \ 26.14, \ p < 0.001 \\ \hline Awareness \ of \ social \ consequences: \ 2 \ studies, \ N = 121, \ r = 0.21, \ p < 0.01, \ 95\% Cl \ -0.09 \ to \ 0.52, \ Q_w \ = \ 5.14, \ p < 0.05 \\ \hline Awareness \ of \ need \ for \ treatment: \ 3 \ studies, \ N = 236, \ r = 0.16, \ p < 0.01, \ 95\% Cl \ 0.16 \ to \ 0.16, \ Q_w = \ non-significant \\ \hline Awareness \ of \ symptoms: \ 4 \ studies, \ N = 215, \ r = 0.39, \ p < 0.001, \ 95\% Cl \ 0.39 \ to \ 0.39, \ Q_w = \ non-\ significant \\ \hline Awareness \ of \ symptoms \ to \ disorder: \ 4 \ studies, \ N = 175, \ r = 0.21, \ p < 0.01, \ 95\% Cl \ -0.16 \ to \ 0.60, \ Q_w \ = \ 11.26, \ p < 0.05 \\ \hline Attribution \ of \ symptoms \ to \ disorder: \ 4 \ studies, \ N = 175, \ r = 0.21, \ p < 0.01, \ 95\% Cl \ -0.16 \ to \ 0.60, \ Q_w \ = \ 11.26, \ p < 0.05 \\ \hline Attribution \ of \ symptoms \ to \ disorder: \ 4 \ studies, \ N = 175, \ r = 0.21, \ p < 0.01, \ 95\% Cl \ -0.16 \ to \ 0.60, \ Q_w \ = \ 11.26, \ p < 0.05 \\ \hline Attribution \ of \ symptoms \ to \ disorder: \ 4 \ studies, \ N = 175, \ r = 0.21, \ p < 0.01, \ 95\% Cl \ -0.16 \ to \ 0.60, \ Q_w \ = \ 11.26, \ p < 0.05 \\ \hline Attribution \ of \ symptoms \ to \ disorder: \ 4 \ studies, \ N = 175, \ r = 0.21, \ p < 0.01, \ 95\% Cl \ -0.16 \ to \ 0.60, \ Q_w \ = \ 11.26, \ p < 0.05 \ \ disorder: \ 4 \ studies, \ N = \ 126, \ p < 0.05 \ \ disorder: \ 4 \ studies, \ N = \ 126, \ p < 0.05 \ \ disorder: \ 4 \ studies, \ N = \ 126, \ p < 0.05 \ \ disorder: \ 4 \ studies, \ N = \ 126, \ p < 0.05 \ \ disorder: \ 4 \ studies, \ N =$

Cognition and symptoms



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12.25, <i>p</i> < 0.01	
Consistency	Inconsistent for all measures except for awareness of social consequences for global, positive and negative symptoms; awareness of the need for treatment for all symptoms; awareness of symptoms for all symptoms; and attribution of symptoms for global and negative symptoms.
Precision	Precise for all measures except the composite measure for global and negative symptoms; overall insight for positive and depressive symptoms; awareness of the mental disorder for positive and depressive symptoms; attribution of symptoms to the disorder for positive and depressive symptoms; and awareness of social consequences for depressive symptoms.
Directness	Direct

Nieuwenstein M, Aleman A, de Haan E

Relationship between symptom dimensions and neurocognitive functioning in schizophrenia: a meta-analysis of WCST and CPT studies

Journal of Psychiatric Research 2001; 35: 119-125

View review abstract online

Comparison	Association between executive functioning, sustained attention and symptom dimensions in people with schizophrenia.
	Note: For WCST-PE, positive correlations indicate an association between increased symptoms and worse performance, and for the CPT- <i>d'</i> , positive correlations indicated increased symptoms were associated with better performance.
Summary of evidence	High quality evidence (medium to large samples, direct, consistent, precise) shows a medium association between increased negative or disorganised symptoms and impaired executive functioning and a medium association between negative symptoms and impaired attention.
	No significant association is reported with positive symptoms or reality distortion or between attention and disorganised symptoms.

Cognition and symptoms



Negative symptoms

A medium positive association suggests that as negative symptoms increase in patients with schizophrenia, they may demonstrate more perseveration errors on the WCST-PE;

15 studies, N = 699, r = 0.27, 95%Cl 0.13 to 0.40, p < 0.01, $Q_w = 18.9$, p > 0.10

A medium negative association suggests that as negative symptoms increase in patients with schizophrenia, they may also demonstrate worse performance on the CPT-d;

6 studies, N = 250, r = -0.31, 95%Cl -0.41 to 0.21, p < 0.01, Q_w = 6.8, p > 0.10

Disorganised symptoms

A medium positive association suggests that as disorganised symptoms increase in patients with schizophrenia, they may demonstrate more perseveration errors on the WCST-PE;

6 studies, N = 273, r = 0.25, 95%CI 0.24 to 0.26, p < 0.01, Q_w = 6.0, p > 0.10

No significant association was reported between disorganised symptoms and attention on CPT-d;

2 studies, N = 98, r = -0.06, 95%CI -0.04 to 0.08, p > 0.05, Q_w = 1.1, p > 0.10

Positive symptoms

No association was reported between positive symptoms and executive functioning on the WCST-PE;

9 studies, N = 487, *r* = 0.06, 95%CI -0.15 to 0.27, *p* > 0.05, Q_w = 13.3, *p* > 0.10

No association was reported between positive symptoms and attention on the CPT-d;

4 studies, N = 188, r = -0.01, 95%CI -0.10 to 0.09, p > 0.05, Q_w = 4.5, p > 0.10

Reality distortion

No significant association reported between reality distortion symptoms and executive functioning on the WCST-PE;

4 studies, N = 194, r = 0.04, 95%Cl -0.22 to 0.30, p > 0.05, $Q_w = 7.4$, p > 0.10

No significant association was reported between reality distortion symptoms and attention on CPT-

d;

2 studies, N = 98, r = 0.04, 95%CI 0.02 to 0.06, p > 0.05, Q_w = 0.0, p > 0.10

Consistency	Consistent
Precision	Precise
Directness	Direct

NeuRA Cognition and symptoms

Cognition and symptoms



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Palmer BW, Savla GN

The association of specific neuropsychological deficits with capacity to consent to research or treatment

Journal of the International Neuropsychological Society 2007; 13: 1047-1059

View review abstract online

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Comparison	Association between neuropsychological performance and capacity to consent to treatment and research in people with schizophrenia spectrum disorders, in terms of their understanding of the information; appreciation of the context; and reasoning of the consequences of their decision.
Summary of evidence	Moderate quality evidence (mostly large samples direct, unable to assess precision or consistency,) suggests impaired understanding and appreciation are more consistently associated with more severe psychopathology, particularly negative symptoms.

Neuropsychological performance

Five studies (N = 1,680) examined the association between an individual's capacity to consent, and their neuropsychological performance. Capacity to consent was assessed in terms of understanding, appreciation and reasoning, in the context of consent to either treatment or research.

Understanding was significantly associated with symptom severity;

3 of 5 studies reported a very small but significant negative association between understanding and severity of general psychopathology, N = 1,542, r = -0.06 to -0.48, p < 0.05

3 of 4 studies reported a small, significant negative association between understanding and negative symptom severity, N = 1,542, r = -0.14 to -0.50, p < 0.05

1 of 5 studies reported a medium-size significant negative association between understanding and positive symptom severity, N = 30, r = -0.38. p < 0.05

Appreciation was significantly associated with symptom severity;

- 2 of 5 studies reported a significant negative association between appreciation and severity of general psychopathology, N = 1,472, r = -0.06 to -0.47, p < 0.05
- 1 of 4 studies reported a small but significant negative association between appreciation and negative symptom severity, N = 1,447 schizophrenia, r = -0.12, p < 0.01

1 of 5 studies reported a medium-size significant negative association between appreciation and positive symptom severity, N = 30, r = -0.37, p < 0.01

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Reasoning was significantly associated with symptom severity;	
1 of 5 studies reported a significant large negative association between reasoning and general psychopathology, N = 30, r = -0.47, p < 0.05	
1 of 4 studies reported a small but significant negative association between reasoning and negative symptom severity, N = 1,447 schizophrenia, r = -0.09, p < 0.001	
1 of 5 studies reported a significant large negative association between reasoning and positive symptom severity, N = 30, r = -0.52, p < 0.05	
Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Pelletier M, Achim AM, Montoya A, Lal S, Lepage M

Cognitive and clinical moderators of recognition memory in schizophrenia: a meta-analysis

Schizophrenia Research 2005; 74: 233-252

View review abstract online

Comparison	Association between recognition memory and symptoms in people with schizophrenia vs. controls.	
Summary of evidence	Moderate quality evidence (large samples, direct, unable to assess consistency or precision) suggests no association between performance on recognition tasks and symptoms.	
Recognition memory and symptoms		
No association between symptoms and effect sizes of recognition memory performance by schizophrenia vs. controls;		
Positive symptoms		
SAPS global ratings: 10 studies, N = 918, $p = 0.12$		
SAPS total items: 7 studies, N = 370, $p = 0.44$		
PANSS positive scale: 6 studies, N = 395, $p = 0.052$		
Negative symptoms		
SANS global ratings: 10 studies, N = 918, $p = 0.07$		

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SANS total items: 8 studies, N = 374, $p = 0.34$		
PANSS negative scale: 6 studies, N = 395, $p = 0.17$		
Overall symptoms		
BRPS: 16 studies, N = 1,158, <i>p</i> = 0.13		
PANSS overall: 8 studies, N = 549, $p = 0.06$		
Consistency	Unable to assess; no measure of consistency is reported	
Precision	Unable to assess; no measure of precision is reported	
Directness	Direct	

Pickup GJ

Relationship between Theory of Mind and executive functioning in schizophrenia: A systematic review

Psychopathology 2008; 41: 206-213

View review abstract online

Comparison	The association between Theory of Mind (ToM), executive functioning and symptoms in people with schizophrenia vs. controls (healthy and various control groups).
Summary of evidence	Moderate to low quality evidence (small samples, direct, unable to assess consistency or precision) suggests impaired performance on various Theory of Mind and executive functioning tasks may be associated with greater overall symptoms severity.

Association with symptoms

Poorer ToM performance was associated with greater severity of negative symptoms (2 studies, N = 107), positive symptoms (1 study, N = 40), paranoid symptoms (1 study, N = 63), poor insight (1 study, N = 55), behavioural problems (1 study, N = 60), disorganised symptoms (2 studies, N = 94), psychomotor poverty (1 study, N = 52) and positive formal thought disorder (3 studies, N = 236). However, two studies reported that ToM was not associated with general symptoms (N = 127), negative symptoms (N = 56) or paranoid symptoms (1 study, N = 56).

Increased negative and positive symptom severity was associated with poorer performance on the hinting task (1 study, N = 50), and increased negative symptoms were associated with poorer

Cognition and symptoms



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picture sequencing and capture errors performance (1 study, $N = 56$).	
Poorer executive function was associated with increased negative thought disorder (1 study, N = 45). No association between executive functioning and symptom severity (2 studies, N = 93).	
Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Pomarol-Clotet E, Oh TM, Laws KR, McKenna PJ		
Semantic priming in schizophrenia: systematic review and meta-analysis		
The British Journal of Psychiatry 2008; 192: 92-97 View review abstract online		
Comparison	Semantic priming in people with schizophrenia with or without thought disorder vs. controls.	
Summary of evidence	Moderate to high quality evidence (unclear sample size, direct, consistent, precise) shows no effect of overall priming in schizophrenia. Moderate quality evidence (inconsistent) suggests a small effect of increased semantic priming, but only in patients with thought disorder.	
Priming		
No difference in overall p	riming in people with schizophrenia (with or without thought disorder) compared with controls;	
36 studies, $d = 0.07$, 95%Cl -0.02 to 0.16, $Q_w = 59.92$, $p = 0.008$		
Authors state that excluding two outliers gave similar results but reduced heterogeneity to NS		
A small effect size suggests significantly increased semantic priming in people with schizophrenia with thought disorder compared with controls;		
18 studies, <i>d</i> = 0.16, 95%CI 0.01 to 0.31, Q _w = 52.31, <i>p</i> < 0.001		
No difference in semantic priming in:		
People with schizophrenia without thought disorder vs. controls;		
14 studies, $d = 0.00$, 95%Cl -0.15 to 0.16, $Q_w = 21.29$, $p = 0.07$		
People with schizophrenia with thought disorder vs. people with schizophrenia without thought		

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disorder;		
13 studies, $d = 0.06$, 95%Cl -0.12 to 0.24, $Q_w = 28.79$, $p = 0.004$		
A small effect size suggests significantly increased indirect semantic priming in people with schizophrenia (with or without thought disorder) compared with controls;		
9 studies	s, $d = 0.19$, 95%Cl 0.03 to 0.36, $Q_w = 4.67$, $p = 0.80$	
A medium effect size suggests significantly increased indirect semantic priming in people with schizophrenia with thought disorder compared with controls;		
6 studies	6 studies, $d = 0.56$, 95%CI 0.31 to 0.80, $Q_w = 7.74$, $p = 0.17$	
A significant difference was reported between patients with thought disorder compared with controls for short Stimulus Onset Asynchronicity (SOA) (10 studies, $d = 0.25$) and long SOA (7 studies, $d = -0.14$), $Q_B = 6.33$, $p = 0.01$.		
A trend difference between patients with thought disorder compared with patients without thought disorder for short SOA (8 studies, $d = 0.15$) and long SOA (6 studies, $d = -0.17$), $Q_B = 3.39$, $p = 0.06$.		
Age and duration of illness showed no effect.		
Consistency	Consistent for overall priming (without outliers) and indirect semantic priming	
Precision	Precise	
Directness	Direct	

Rajji TK, Mulsant BH

Nature and course of cognitive function in late-life schizophrenia: a systematic review

Schizophrenia Research 2008; 102: 122-140

View review abstract online

Comparison	Association between cognitive functioning and symptoms dimensions in people with schizophrenia aged over 50 years (late-life schizophrenia, LLS).
Summary of evidence	Moderate to low quality evidence (medium-sized sample, unable to assess consistency or precision, direct) is unclear about associations between cognitive deficits and positive and negative symptoms in late-life schizophrenia.

Cognition and symptoms



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Negative symptoms

One study (N = 330) reported that people with LLS performed more poorly than ethnic and premorbid functioning matched controls and that increased negative symptoms in patients correlated with poor performance on all measures of the CERAD (animal fluency, BNT, Praxis, word-list learning, recall and recognition).

Positive symptoms

One study (N = 330) reported that people with LLS performed more poorly than ethnic and premorbid functioning matched controls and that increased positive symptoms in patients correlated with poor performance on praxis (practicing).

Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Reinharth J, Reynolds G, Dill C, Serper M

Cognitive predictors of violence in schizophrenia: a meta-analytic review

Schizophrenia Research, Cognition 2014; 1: 1101-111

View review abstract online

Comparison	Association between aggression and cognition in people with a psychotic disorder (inpatients or outpatients).
	85.9% of the sample had a diagnosis of a psychotic disorder; ~70% had schizophrenia or schizoaffective disorder.
Summary of evidence	Moderate to high quality evidence (large samples, inconsistent, precise, direct) suggests a small, decreased risk of aggression with better cognitive performance. High quality evidence (consistent) suggests this effect is apparent for global cognition and insight. There were no significant relationships with memory, attention, executive functioning, or visual-spatial reasoning (trend effect).
Aggression	

Cognition and symptoms



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Small, decreased risk of aggression with better cognitive performance; 29 studies, N = 4,764, OR 0.59, 95%CI 0.51 to 0.67, p < 0.05, I² = 63.72, p < 0.05 Subgroup analyses showed similar effect sizes according to; Combined measures of insight, general cognition, attention, visual-spatial reasoning, memory, motor functioning and processing speed: 19 studies, N = 3,507, OR 0.72, 95%Cl 0.63 to 0.82, $p < 10^{-10}$ 0.05, l² < 25%, *p* > 0.05 Global cognition: 11 studies, N = 732, OR 0.61, 95%CI 0.47 to 0.80, p < 0.05, $l^2 < 25\%$, p > 0.05Insight: 5 studies, N = 2,422, OR 0.72, 95%CI 0.61 to 0.86, p < 0.05, $l^2 < 50\%$, p > 0.05Small, increased risk of aggression with better motor functioning; Motor functioning: 4 studies, N = 370, OR 1.52, 95%CI 1.03 to 2.24, p < 0.05, $l^2 < 25\%$, p > 0.05Authors report no significant relationships between aggression and executive functioning (r = 0.01, p > 0.05) visual-spatial reasoning (r = -0.13, p = 0.06), memory (r = -0.09, p > 0.05) or attention (r = -0.13, p = 0.06), memory (r = -0.09, p > 0.05) or attention (r = -0.13, p = -0.06), memory (r = -0.09, p > 0.05) or attention (r = -0.06), memory (r = -0.09, p > 0.05) or attention (r = -0.06), memory (r = -0.09, p > 0.05) or attention (r = -0.06). -0.08, p > 0.05). Authors report no publication bias **Consistency in results** Consistent for subgroup analyses only Precision in results Precise apart from motor functioning **Directness of results** Direct

So S, Garety P, Peters E, Kapur S

Do antipsychotics improve reasoning bias? A review

Psychosomatic Medicine 2010; 72:681-693

View review abstract online

Comparison	Association between performance on Theory of Mind (ToM) and reasoning bias tasks and symptoms in people with schizophrenia.
Summary of evidence	Moderate quality evidence (small samples, direct, unable to assess precision, appears consistent) suggests performance on Theory of Mind tasks may be associated with negative and total scores on the PANSS and SANS, with positive symptoms showing a weaker association. Moderate to low quality evidence (small samples, direct, unable

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	to assess precision, appears inconsistent) suggests performance on Theory of Mind stories may be related to delusional outcome (preoccupation and distress). Moderate quality evidence (small samples, direct, unable to access precision, mostly consistent) suggests an associated between more severe positive symptoms (usually delusions) and greater belief inflexibility, internalising, externalising and personalising attribution bias. Moderate to low quality evidence (small samples, direct, unable to access precision, appears inconsistent) is unable to determine any clear relationships between JTC or evidence evaluation and schizophrenia, nor the effects of antipsychotics on JTC or attribution style.
	Theory of Mind and symptom severity
1 observational study, N = 128 (medication not reported), measured performance on a hinting task. ToM performance correlated with PANSS positive, negative and delusion scores, with increased performance being related to reduction in symptoms. Patients with disorganised symptoms tended	
to perform worse than those with positive and negatives symptoms. 1 observational study, N = 77 (22 patients on antipsychotics vs. 55 controls), measured performance on a computerised mental inference task.	
Affective ToM was associated with negative symptoms (SANS alogia, SANS attention and SANS total symptoms), whereas cognitive ToM was associated with positive symptoms (PANSS). The authors concluded that ToM performance was more strongly related to negative symptoms and thought disorder than to positive symptoms.	
1 observational study, N = 71 (on atypical (88.6%) and typical (11.4%) antipsychotics), measured performance on a hinting task.	
ToM performance correlated with PANSS negative symptoms, general and total score, but not positive score on the PANSS.	
1 observational study, N = 128 (39 currently paranoid, 29 remitted paranoid, 27 non-psychotic depressed, 33 healthy controls), measured performance on ToM stories.	
Patients with persecutory delusions scored lower on the ToM task. Performance on ToM stories correlated significantly with delusional preoccupation and distress, but the picture-sequencing task did not and there was no correlation with antipsychotic dosage.	
1 observational study, N = 21 (10 fully remitted, 5 partially remitted, 6 acutely deluded), 15 patients were on antipsychotics, measured performance on a picture-sequencing task and ToM questionnaire.	
No group differences, authors concluded that ToM performance was not related to severity of delusions, which could be due to the small sample.	

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Jumping to conclusions, attributional style, belief flexibility and evidence evaluation

Jumping to conclusions (JTC)

1 longitudinal study (N = 19 with current hallucinations or delusions) reported that greater delusion symptom scores were associated with poorer performance on the fish task with earlier termination of information gathering.

1 observational study (N = 81: 23 with delusions, 22 psychiatric controls, 36 healthy controls) reported that greater positive and delusional symptoms were associated with fewer beads drawn, and anxiety disorder was associated with a greater number of beads drawn on the Beads task.

1 observational study (N = 100 with current delusions) reported a trend effect of greater positive and delusional symptoms (measured by PANSS) being associated with poorer performance on the Beads task.

No association was reported between severity of delusional symptoms and change in number of 'draws to decision' (1 observational study, N = 19), or JTC performance (1 observational study, N = 128 with schizophrenia, and 1 longitudinal study N = 55: 17 with delusions, 18 psychiatric controls, 20 controls).

Attribution style

1 observational study (N = 81: 23 with delusions, 22 psychiatric controls, 36 healthy controls) reported that deluded patients made significantly more internalizing attributions than healthy controls. Patients with "bad me" delusions showed the greatest self-serving bias and patients with "poor me" delusions showed a depressive attributional style. No association was reported between attribution style and clinical measures at baseline.

 observational study (N = 136: 40 with acute delusions, 25 with remitted delusions, 35 depressed, 36 healthy controls) reported that people with acute delusions showed significantly greater personalizing bias than patients with remitted delusional symptoms. All patients with delusions (acute or remitted) showed externalizing bias for negative events. Greater attribution bias was significantly associated with increased symptom severity.

- 1 observational study (N = 71 with schizophrenia) reported that people with increased persecutory and grandiose beliefs showed greater externalizing attribution for negative events.
- 1 longitudinal study (N = 55: 17 with delusions, 18 psychiatric controls, 20 healthy controls) reported an increase in self-serving bias at follow-up across all groups.

1 observational study (N = 86 with schizophrenia) reported that greater overall psychopathology was associated with less externalizing bias, however no association was reported between externalizing or internalizing bias and delusions specifically.

Belief flexibility

1 observational study (N = 100 with current delusions) reported that poorer belief flexibility was associated with greater delusional symptoms. No association was reported between belief flexibility and severity of psychosis.

1 observational study (N = 100 with current delusions) reported that poorer belief flexibility was

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associated with greater delusional symptoms and hallucinations (measured by PANSS). No association was reported between belief flexibility and negative or general symptoms.

1 observational study (N = 76: 36 with active delusions, 16 with remitted delusions, 24 healthy controls) reported that patients with active delusions were less responsive to disconfirmatory evidence than remitted patients.

1 observational study (N = 69: 17 with delusions, 17 without delusions, 35 healthy controls) reported that the deluded and non-deluded groups showed poorer belief flexibility compared with controls, with only the comparison between non-deluded and controls reaching significance. No association was reported between groups on personally meaningful beliefs.

Evidence evaluation

1 longitudinal study (N = 95: 29 schizophrenia, 31 anxious, 35 healthy controls) reported no association between individual psychiatric symptom severity and performance on a probability judgment task, however the effect of confirmatory and disconfirmatory evidence on probability judgment was stronger in remitted patients than non-remitted patients.

Consistency	Unable to assess; no measure of consistency is reported
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Ventura J, Helleman GS, Thames AD, Koellner V, Nuechterlein KH

Symptoms as mediators of the relationship between neurocognition and functional outcome in schizophrenia: a meta-analysis.

Schizophrenia Research 2009; 113(2-3): 189-99

View review abstract online

Comparison	Associations between positive, negative symptoms and cognitive functioning in people with schizophrenia.
Summary of evidence	Moderate quality evidence (large samples, direct, inconsistent, unable to assess precision) suggests that increased negative symptoms (but not positive symptoms) are significantly associated with reduced global cognitive functioning, working memory, speed of processing, verbal learning and memory, reasoning and problem solving, attention, and visual learning and memory.
Positive Symptoms	

Cognition and symptoms



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No significant association was reported between positive symptom severity and overall cognitive functioning;	
25 studies, N = 1,297, <i>r</i> = -0.00, <i>p</i> = 0.97	
Individual domains of cognit	ive function also failed to show any significant association with positive symptom severity;
Workir	ng memory: 8 studies, N = 357, r = -0.03, p = 0.54
Speed of	processing: 18 studies, N = 1,040, r = 0.04, p = 0.21
Verbal learni	ng and memory: 10 studies, N = 531, r = 0.00, p = 0.93
Reasoning an	d problem solving: 16 studies, N = 797, $r = 0.00$, $p = 0.94$
Attentio	n / vigilance: 4 studies, N = 199, <i>r</i> = -0.10, <i>p</i> = 0.15
Visual learni	ing and memory: 4 studies, N = 197, r = -0.10, p = 0.20
Negative Symptoms	
Medium effect size suggests a significant association between increased negative symptom severity and reduced overall cognitive functioning;	
53 studies, N = 4929, <i>r</i> = -0.24, <i>p</i> < 0.01	
Small effect sizes suggest significant relationships between increased negative symptoms and poorer cognitive performance in;	
Working memory: 17 studies, N = 2,230, <i>r</i> = -0.21, <i>p</i> < 0.01	
Speed of processing: 33 studies, N = 3,899, $r = -0.26$, $p < 0.01$	
Verbal learning and memory: 23 studies, N = 2,978, r = -0.21, p < 0.01	
Reasoning and problem solving: 27 studies, N = 3,039, r = -0.13, p < 0.01	
Attention/ vigilance: 10 studies, N = 2,138, r = -0.17, p < 0.01	
Visual learning and memory: 8 studies, N = 454, r = -0.16, p < 0.01	
Consistency	Authors report all results are inconsistent
Precision	Unable to assess; no measure of precision is reported
Directness	Direct

Ventura J, Thames AD, Wood RC, Guzik LH, Hellemann G

Disorganisation and reality distortion in schizophrenia: a meta-analysis of

NeuRA Cognition and symptoms



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the relationship between positive symptoms and neurocognitive deficits Schizophrenia Bulletin 2010; 121(1-3): 1-14 View review abstract online Comparison Association between reality distortion, disorganised symptoms and cognitive functioning in people with schizophrenia. Summary of evidence Moderate to high quality evidence (large samples, direct, inconsistent, precise) suggests a small effect that overall reduced cognitive functioning may be associated with both disorganised and reality distortion symptoms. Disorganised symptoms may be specifically associated with reductions in attention/vigilance, reasoning and problem solving, speed of processing, verbal memory, working memory and visual memory. Reality distortion may be specifically associated with reduced attention/vigilance, and reasoning and problem solving. Disorganised symptoms and reality distortion combined Small effect size suggests a significant relationship between increased disorganised symptoms and reality distortion combined, and reduced cognitive functioning; 40 studies, N = 4,654, r = -0.05, p < 0.01, CI not reported **Disorganised symptoms** Medium effect size suggests a significant association between increased disorganised symptoms and reduced overall cognitive functioning; 69 studies, N = 4,002, r = -0.23, 95%CI -0.26 to -0.20, p < 0.01 Medium effect sizes suggest significant associations between increased disorganised symptoms and reduction in the following cognitive functions; Attention/ vigilance: 19 studies, N = 1,404, r = -0.25, 95%CI -0.31 to -0.20, p < 0.01 Reasoning and problem solving: 38 studies, N = 2,300, r = -0.24, 95%Cl -0.28 to -0.19, p < 0.01Speed of processing: 42 studies, N = 2,473, r = -0.26, 95%Cl -0.30 to -0.22, p < 0.01Verbal memory: 22 studies, N = 1,532, r = -0.20, 95%CI -0.24 to -0.15, p < 0.01

Working memory: 20 studies, N = 945, r = -0.20, 95%Cl -0.26 to -0.13, p < 0.01

Visual memory: 14 studies, N = 978, *r* = -0.20, 95%CI -0.27 to -0.14, *p* < 0.01

Reality distortion

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Very small effect size suggest significant associations between increased reality distortion and reduced overall cognitive functioning; 50 studies, N = 2,722, r = -0.04, 95%CI -0.08 to -0.01, p = 0.03 Very small effect sizes suggest significant associations between increased reality distortion and reduced cognitive functions in; Attention/ vigilance: 10 studies, N = 743, r = -0.12, 95%CI -0.19 to -0.05, p < 0.01 Reasoning and problem solving: 27 studies, N = 1,427, r = -0.06, 95%Cl -0.11 to -0.05, p = 0.03No significant relationships between reality distortion and; Speed of processing: 33 studies, N = 1,870, r = -0.03, 95%CI -0.07 to 0.02, p = non-significantVerbal memory: 16 studies, N = 927, r = 0.01, 95%CI -0.07 to 0.06, p = non-significant Working memory: 18 studies, N = 855, r = -0.00, 95%CI -0.07 to 0.07, p = non-significantVisual memory: 10 studies, N = 630, r = 0.01, 95%CI -0.07 to 0.09, p = non-significant Consistency Authors report results are inconsistent Precision Precise, unable to assess for combined positive symptoms Directness Direct

Ventura J, Wood RC, Hellemann GS

Symptom Domains and Neurocognitive Functioning Can Help Differentiate Social Cognitive Processes in Schizophrenia: A Meta-Analysis

Schizophrenia Bulletin 2013; 39(1): 102-111

View review abstract online

Comparison	Association between social cognition, symptom domains and cognitive functioning in people with schizophrenia.
Summary of evidence	Moderate quality evidence (medium to large samples, consistent, direct, unable to assess precision) suggests small to medium size associations between poor performance on emotion perception, social perception and Theory of Mind tasks and increased symptoms.
Associatio	ns between social cognition and symptom domains

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Small to medium size	Small to medium size associations between poor emotion perception and increased;	
Reality distortion: 18 studies, N = 757, r = -0.22, Q _w = 44.22, p < 0.001		
Omitting 2 studies gave homogenous results and $r = -0.21$		
Disorganization: 22 studies, N = 987, r = -0.32, Q _w = 42.33, p = 0.01		
Omitting 2 studies gave homogenous results and $r = -0.34$		
Negative symptoms: 53 studies, N = 2,303, r = -0.26, Q _w = 109.70, p < 0.001		
Omitting 8 studies gave homogenous results and $r = -0.30$		
Combined reality distortion/disorganization: 17 studies, N = 771, r = -0.17, Q_w = 6.99, p = 0.98		
Small to medium size associations between poor social perception and increased;		
Reality distortion: 6 studies, N = 182, r = -0.21, Q _w = 13.34, p = 0.04		
Omitting 1 study gave homogenous results and $r = -0.37$		
Disorganization: 7 studies, N = 228, r = -0.22, Q _w = 10.55, p = 0.16		
Negative symptoms: 18 studies, N = 952, r = -0.20, Q _w = 37.64, p < 0.001		
Omitting 1 study gave homogenous results and $r = -0.22$		
Combined reality distortion/disorganization: 11 studies, N = 684, r = -0.11, Q _w = 33.49, p < 0.001		
Omitting 1 study gave homogenous results and $r = -0.16$		
Small association between poor attribution bias and increased;		
Reality distortion: 6 studies, N = 250, r = -0.07, Q _w = 25.87, p = 0.01		
Omitting 2 studies gave homogenous results and $r = -0.06$		
Small to medium size associations between poor Theory of Mind and increased;		
Reality distortion: 14 studies, N = 624, r = -0.08, Q _w = 15.50, p = 0.34		
Disorganization: 16 studies, N = 684, r = -0.32, Q _w = 19.14, p = 0.26		
Negative symptoms: 38 studies, N = 1,869, r = -0.25, Q _w = 43.43, p = 0.25		
Combined reality distortion/disorganization: 15 studies, N = 583, r = -0.22, Q _w = 13.28, p = 0.58		
Consistency in results	Consistent	
Precision in results	Unable to assess; no measure of precision is reported	
Directness of results	Direct	

Ventura J, Wood RC, Jimenez AM, Hellemann GS

Neurocognition and symptoms identify links between facial recognition

NeuRA Cognition and symptoms

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and emotion process	ing in schizophrenia: Meta-analytic findings	
Schizophrenia Research 2	013: 151: 78-84	
View review abstract online		
Comparison	Association between social cognition, symptom domains and cognitive functioning in people with schizophrenia.	
Summary of evidence	Moderate quality evidence (mostly medium-sized samples, consistent, unable to assess precision, direct) suggests small to medium size associations between poor facial recognition and emotion processing and increased symptoms.	
Association	ns between social cognition and symptom domains	
Small to medium si	ze associations between poor facial recognition and increased;	
Reality disto	prtion: 4 studies, N = 203, r = -0.02, Q _w = 1.99, p = 0.74	
Disorganization: 5 studies, N = 240, r = -0.25, Q _w = 3.49, p = 0.62		
Negative symp	ptoms: 12 studies, N = 487, r = -0.22, Q _w = 20.44, p = 0.06	
Combined reality distortion	on/disorganization: 3 studies, N = 138, r = -0.25, Q _w = 0.80, p = 0.85	
Small to medium size associations between poor emotion processing (facial stimuli) and increased;		
Reality distortion: 18 studies, N = 757, r = -0.21, Q _w = 45.70, p < 0.001		
Omitting 2 studies gave homogenous results and $r = -0.20$		
Disorganization: 22 studies, N = 987, $r = -0.32$, $Q_w = 39.21$, $p = 0.01$		
Omitting 1 study gave homogenous results and $r = -0.33$		
Negative sympto	ms: 53 studies, N = 2,825, <i>r</i> = -0.25, Q _w = 132.35, <i>p</i> < 0.001	
Omitting	10 studies gave homogenous results and $r = -0.28$	
Combined reality distortion	/disorganization: 22 studies, N = 1,076, r = -0.18, Q _w = 34.23, p = 0.05	
Omitting 1 study gave homogenous results and $r = -0.16$		
Small to medium size associations between poor emotion processing (voice prosody) and increased;		
Reality distortion: 2 studies, N = 81, r = -0.31, Q _w = 0.64, p = 0.73		
Disorganiza	Disorganization: 3 studies, N = 124, r = -0.47, Q _w = 8.90, p = 0.03	
Omitting 1 study gave homogenous results and $r = -0.60$		
Negative symptoms: 7 studies, N = 312, r = -0.25, Q _w = 8.52, p = 0.29		
Combined reality distortion/disorganization: 1 study, N = 36, r = -0.13, Q _w = N/A		



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Consistency in results	Consistent
Precision in results	Unable to assess; no measure of precision is reported
Directness of results	Direct

Wang Y, Cui J, Chan R, Deng Y, Shi H, Hong X, Li Z, Yu X, Gong QY, Shum D

Meta-analysis of prospective memory in schizophrenia: Nature, extend, and correlates

Schizophrenia Research 2009; 114: 64-70

View review abstract online

Comparison	Prospective memory (time-based, event-based and activity- based prospective memory) in people with schizophrenia vs. controls.
	Note: Prospective memory (PM) is the ability to remember to carry out an intended action in the future.
Summary of evidence	Moderate to high quality evidence (small to medium-sized samples, consistent, precise, direct,) suggests a significant, small association between poorer prospective memory and increased general psychopathology. No association was reported between prospective memory and positive symptoms.
	Moderate quality evidence (inconsistent) suggests a significant, small association between poorer prospective memory and increased negative symptoms.
Prospective memory	

A significant, small association was reported between impaired prospect memory and increased general psychopathology and negative symptoms;

General psychopathology: 4 studies, N = 146, r = -0.168, 95%CI -0.326 to 0, p = 0.05, Q_w = 2.268, p = 0.519

Negative symptoms: 8 studies, N = 400, r = -0.18, 95%CI -0.276 to -0.081, p < 0.001, Q_w = 21.32, p = 0.003

No association was reported with positive symptoms;

8 studies, N = 400, r = -0.094, 95%CI -0.193 to 0.007, p = 0.067, Q_w = 7.512, p = 0.378





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Consistency	Consistent for all measures except negative symptoms
Precision	Precise
Directness	Direct

Waters F, Woodward T, Allen P, Aleman A, Sommer I

Self-recognition deficits in schizophrenia patients with auditory hallucinations: a meta-analysis of the literature

Schizophrenia Bulletin 2012; 38(4): 741-750

View review abstract online

Comparison	Self-recognition in people with schizophrenia with auditory hallucinations in the week prior to testing vs. those without auditory hallucinations in the week prior to testing.
Summary of evidence	Moderate quality evidence (small to medium-sized samples, consistent, unable to assess precision, direct) suggests a medium effect of poorer self-recognition, but not new item recognition, in people with schizophrenia with auditory hallucinations compared with people with schizophrenia without auditory hallucinations.
Self-recognition and new item recognition	
Significant medium effect of poorer self-recognition, but not new item recognition, in people with schizophrenia with auditory hallucinations compared with people with schizophrenia without auditory hallucinations;	
Self-recognition accuracy: 9 studies, N = 315, g = -0.58, CI not reported, p < 0.00001, I ² = 17%	
New item recognition: 5 studies, N = 214, g = -0.13, CI not reported, $p = 0.352$, I ² = 71%	
No evidence of publication bias	
Consistency in results	Consistent for self-recognition accuracy
Precision in results	Unable to assess; no measure of precision is reported
Directness of results	Direct

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Explanation of acronyms

B = estimated regression coefficient, BADE = Bias Against Disconfirmatory Evidence task, BNT = Boston Naming Test, BPRS = Brief Psychiatric Rating Scale, CERAD = Consortium to Establish Registry for Alzheimer's Disease, CDR = Clinical Dementia Rating scale, CI = Confidence Interval, B = regression coefficient, CPT – d' = Continuous Performance Task, measure of sensitivity, d =Cohen's d = standardised mean differences (see below for interpretation of effect size), ES = effect size (unspecified), l^2 = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), IQ = Intelligence Quotient, JTC = Jumping to Conclusions, LLS = late-life schizophrenia, MMSE = Mini-Mental Status Examination, N = number of participants, NS = non-significant, p = statistical probability of obtaining that result (p < 0.05generally regarded as significant), PANSS = Positive and Negative Symptoms Scale, Q = Q statistic for the test of heterogeneity, $Q_w =$ test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency), Q_B = test for between group differences (heterogeneity between groups of studies for an outcome of interest), r = correlation coefficient, RCT = randomised controlled trial, SAI-E = Schedule for Assessing the 3 components of insight – Expanded Version, SANS = Scale for the Assessment of Negative Symptoms, SAPS = Scale for the Assessment of Positive Symptoms, SE = standard error, SOA = Stimulus Onset Asynchrony, ToM = Theory of Mind, μ_p = estimated average correlation in the population, vs. = versus, WCST = Wisconsin Card Sorting Task, WCST-PE = Wisconsin Card Sorting Task, perseveration error

Cognition and symptoms



Explanation of technical terms

- Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias - selective reporting of results; publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias - only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small³².
- † Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation. Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect³².

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2^{33} . InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios

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measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, r) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An r of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents а strong association. Unstandardised (b) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable. statistically controlling for the other independent Standardised variables. regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. I² is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity. I² can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;³²

$$|^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

- Imprecision refers to wide confidence § intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed.34
- Indirectness of comparison occurs when a comparison of intervention A versus B is not available but A was compared with C and B was compared with C that allows indirect comparisons of the magnitude of effect of A Indirectness of versus B. population. comparator and/or outcome can also occur when the available evidence regarding a particular population, intervention. comparator, or outcome is not available and is therefore inferred from available evidence. These inferred treatment effect sizes are of lower quality than those gained from head-tohead comparisons of A and B.

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